

CLAIMS

1. A targeting molecule linked to at least one biological agent wherein said targeting molecule comprises a polypeptide that:

- (a) forms a closed covalent loop; and
- (b) contains at least three peptide domains having  $\beta$ -sheet character, each of the domains being separated by domains lacking  $\beta$ -sheet character wherein said polypeptide is not full length dimeric IgA.

2. A targeting molecule according to claim 1 wherein said targeting molecule is covalently linked to at least one biological agent.

3. A targeting molecule according to claim 2 wherein said molecule contains at least one cysteine residue linked to the biological agent(s).

4. A targeting molecule according to claim 2 wherein said molecule is linked to a biological agent via a peptide bond.

5. A targeting molecule according to claim 1 wherein said molecule is noncovalently linked to at least one biological agent.

6. A targeting molecule according to claim 1 wherein said polypeptide comprises amino acid residues 13-71 and 93-101 of SEQ ID NO:1, amino acid residues 13-71 and 93-99 of SEQ ID NO:2, amino acid residues 12-70 and 92-101 of SEQ ID NO:3, amino acid residues 12-70 and 92-100 of SEQ ID NO:4, amino acid residues 11-69 and 89-96 of SEQ ID NO:5 and/or amino acid residues 3-61 and 79-88 of SEQ ID NO:6, or a variant thereof that differs only in conservative substitutions and/or modifications.

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7. A targeting molecule according to claim 1 wherein said polypeptide comprises the amino acid sequence recited in SEQ ID NO:7, or a variant thereof that differs only in conservative substitutions and/or modifications.

8. A targeting molecule according to claim 1 wherein said polypeptide comprises the amino acid sequence recited in SEQ ID NO:8, or a variant thereof that differs only in conservative substitutions and/or modifications.

9. A targeting molecule according to claim 1 wherein said polypeptide comprises the amino acid sequence recited in SEQ ID NO:13, or a variant thereof that differs only in conservative substitutions and/or modifications.

10. A targeting molecule according to claim 1 wherein said polypeptide contains at least four peptide domains having  $\beta$ -sheet character, separated by domains lacking  $\beta$ -sheet character.

11. A targeting molecule according to claim 7 wherein said variant comprises amino acid residues 13-99 of SEQ ID NO:2, amino acid residues 12-101 of SEQ ID NO:3, amino acid residues 12-100 of SEQ ID NO:4, amino acid residues 11-95 of SEQ ID NO:5 and/or amino acid residues 3-88 of SEQ ID NO:6, or a variant thereof that differs only in conservative substitutions and/or modifications.

12. A targeting molecule according to claim 1 wherein said polypeptide further comprises a linear N-terminal domain.

13. A targeting molecule according to claim 12 wherein said N-terminal domain comprises amino acid residues 1-12 of SEQ ID NO:1, amino acid residues 1-12 of SEQ ID NO:2, amino acid residues 1-11 of SEQ ID NO:3, amino acid residues 1-11 of SEQ ID NO:4, amino acid residues 1-10 of SEQ ID NO:5, and/or amino acid residues 1-2 of SEQ ID NO:6, or a variant thereof that differs only in conservative substitutions and/or modifications.

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14. A targeting molecule according to claim 1 wherein said polypeptide further comprises a C-terminal domain.

15. A targeting molecule according to claim 14 wherein said C-terminal domain comprises a linear peptide having  $\beta$ -sheet character.

16. A targeting molecule according to claim 12 wherein said linear peptide comprises amino acid residues 102-108 of SEQ ID NO:1, amino acid residues 100-106 of SEQ ID NO:2, amino acid residues 102-108 of SEQ ID NO:3, amino acid residues 101-107 of SEQ ID NO:4 and/or amino acid residues 89-99 of SEQ ID NO:6, or a variant thereof that differs only in conservative substitutions and/or modifications.

17. A targeting molecule according to claim 14 wherein said C-terminal domain comprises a covalently closed loop.

18. A targeting molecule according to claim 17 wherein the covalently closed loop within said C-terminal domain comprises amino acid residues 109-137 of SEQ ID NO:1, amino acid residues 107-135 of SEQ ID NO:2, amino acid residues 109-137 of SEQ ID NO:3, amino acid residues 108-136 of SEQ ID NO:4, amino acid residues 96-119 of SEQ ID NO:5, and/or amino acid residues 100-128 of SEQ ID NO:6, or a variant thereof that differs only in conservative substitutions and/or modifications.

19. A targeting molecule linked to at least one biological agent wherein said targeting molecule is a polypeptide comprising a sequence recited in any one of SEQ ID NO:1 - SEQ ID NO:6.

20. A targeting molecule linked to at least one biological agent wherein said targeting molecule is a polypeptide comprising a sequence recited in SEQ ID NO:7.

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21. A targeting molecule linked to at least one biological agent wherein said targeting molecule is a polypeptide comprising a sequence recited in SEQ ID NO:8.

22. A targeting molecule linked to at least one biological agent wherein said targeting molecule is a polypeptide comprising a sequence recited in SEQ ID NO:13.

23. A targeting molecule according to any one of claims 19-22 wherein said targeting molecule is covalently linked to at least one biological agent.

24. A targeting molecule according to claim 23 wherein said targeting molecule contains at least one cysteine residue linked to the biological agent(s).

25. A targeting molecule according to claim 23 wherein said molecule is linked to a biological agent via a peptide bond.

26. A targeting molecule according to claim 23 wherein said molecule is linked to a biological agent via a glycoside bond.

27. A targeting molecule according to claim 23 wherein said molecule is linked to a biological agent via a phosphodiester bond.

28. A targeting molecule according to any one of claims 19-22 wherein said molecule is noncovalently linked to at least one biological agent.

29. A targeting molecule capable of specifically binding to a basolateral factor associated with an epithelial surface and causing the internalization of a biological agent linked thereto, wherein the targeting molecule is not full length dimeric IgA.

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30. A targeting molecule according to claim 1 or claim 29 wherein said biological agent is selected from the group consisting of enzymes, binding agents, inhibitors, nucleic acids, carbohydrates and lipids.

31. A pharmaceutical composition comprising a targeting molecule linked to at least one biological agent according to claim 1 or claim 29, in combination with a pharmaceutically acceptable carrier.

32. A method for treating a patient afflicted with a disease associated with an epithelial surface, comprising administering to a patient a pharmaceutical composition according to claim 31.

33. A method according to claim 32 wherein said patient is afflicted with a disease selected from the group consisting of cancer, viral infection, inflammatory disorders, autoimmune disorders, asthma, celiac disease, colitis, pneumonia, cystic fibrosis, bacterial infection, mycobacterial infection and fungal infection.

34. A method for inhibiting the development in a patient of a disease associated with an epithelial surface, comprising administering to a patient a pharmaceutical composition according to claim 31.

35. A method according to claim 34 wherein the disease is selected from the group consisting of cancer, viral infection, autoimmune disorders, asthma, celiac disease, colitis, pneumonia, cystic fibrosis, bacterial infection, mycobacterial infection and fungal infection.

36. A targeting molecule linked to at least one biological agent wherein said targeting molecule comprises a polypeptide that:

(a) forms a closed covalent loop; and

(b) contains at least three peptide domains having  $\beta$ -sheet character, each of the domains being separated by domains lacking  $\beta$ -sheet character wherein said targeting molecule is linked to at least one biological agent by a substrate for an intracellular or extracellular enzyme associated with or secreted from an epithelial barrier.

37. A targeting molecule according to claim 36 wherein said enzyme is selected from the group consisting of proteases, glycosidases, phospholipases, esterases, hydrolases, and nucleases.

38. A targeting molecule linked to at least one biological agent wherein said targeting molecule comprises a polypeptide that:

- (a) forms a closed covalent loop; and
- (b) contains at least three peptide domains having  $\beta$ -sheet character, each of the domains being separated by domains lacking  $\beta$ -sheet character wherein said targeting molecule is linked to at least one biological agent through a side chain of amino acids in an antibody combining site.

39. A targeting molecule linked to at least one biological agent wherein said targeting molecule comprises a polypeptide that:

- (a) forms a closed covalent loop; and
- (b) contains at least three peptide domains having  $\beta$ -sheet character, each of the domains being separated by domains lacking  $\beta$ -sheet character wherein the biological agent is not naturally associated with the targeting molecule, and wherein the biological agent is not iodine.

40. A targeting molecule according to claim 39 wherein said biological agent is selected from the group consisting of enzymes, binding agents, inhibitors, nucleic acids, carbohydrates and lipids.

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41. A targeting molecule according to claim 39 wherein said biological agent comprises an antigen combining site.

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